A phase Ib double-blind, placebo-controlled, randomized, dose-escalating trial to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of repeated subcutaneous injections of MT203 in patients with mild to moderate rheumatoind arthritis (RA) on treatment with methotrexate.

Published: 29-10-2010
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Primary objective: Safety and tolerability of repeated subcutaneous injections of MT203 in patients with mild to moderate RA.Secondary objectives: Pharmacokinetics, pharmacodynamics, including explorative biomarker assessments and efficacy of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON38054

Source
ToetsingOnline

Brief title
PRIORA

Condition

- Autoimmune disorders

Synonym
RA, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Takeda
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: methotrexate, rheumatoid arthritis, subcutaneous

Outcome measures

Primary outcome

Not applicable: this is a mainly a safety and efficacy study (phase Ib), please

refer to the study objectives.

Secondary outcome

Not applicable; see primary endpoints.

Study description

Background summary

Rheumatoid arthritis (RA) is a chronic destructive disease characterized by joint inflammation leading to erosions of articular cartilage and subchondral bone.Granulocyte macrophage colony stimulating factor (GM-CSF) is thought to be a key activator of the innate arm of the immune system and as such is involved in chronic stages of inflammatory and autoimmune diseases where macrophages, neutrophils, granulocytes, eosinophils and dendritic cells contribute to disease progression. MT203 is a human IgG1 monoclonal antibody potently and specifically neutralizing GM-CSF. It shows promise for the treatment of autoimmune diseases, such as RA. MT203 appears to be generally safe and

well-tolerated.

Study objective

Primary objective: Safety and tolerability of repeated subcutaneous injections of MT203 in patients with mild to moderate RA.
Secondary objectives: Pharmacokinetics, pharmacodynamics, including explorative biomarker assessments and efficacy of repeated subcutaneous injections of MT203 in patients with mild to moderate RA.

Study design

This is a phase Ib, double-blind, placebo-controlled, randomized, dose-escalating study in approximately 24 subjects in The Netherlands and Bulgaria.

Intervention

Repeated subcutaneous injections of MT203 or placebo, every 14 days (in total 3 doses per patient).

Study burden and risks

Although a first-in-man trial has been performed, the following potential risks cannot be excluded yet: allergic reaction, local pain, haematoma, or a superficial thrombophlebitis, Pulmonary Alveolar Proteinosis (PAP), mild and transient increase in serum transaminase activity levels (ALAT, ASAT) and in serum CRP levels.
As MT203 is expected to have immunomodulatory effects the potential risk of increased infection rates needs to be considered. To safeguard the patients, medical history and signs indicative of predisposition to or presence of underlying latent or incipient infections will be checked during screening and patients having these signs excluded. Patients will be excluded from participation in the trial in case of a positive test or other clinical evidence of tuberculosis.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Out-patients with active RA with low to moderate disease activity (DAS28 >= 2.6 and <= 5.1).
2. Patients must be on stable doses of MTX >= 7.5 and <= 25 mg/week for at least 12 weeks before the first injection of IMP, with appropriate folic acid supplementation.
3. Age >= 18 years at screening.
4. Body weight >= 50 kg at screening; BMI >= 18.0 and <= 30.0 kg/m2 at screening.

Exclusion criteria

1. The use of any medication, including local injections with gold or corticosteroids, over-the-counter medication and prescription anti-rheumatic naturopathic medicines/phytopharmaca ("herbs") with immunomodulatory effect, except for the allowed concomitant medication, within 2 weeks, or within less than 10 times the half-life of the respective drug, or within the duration of its pharmacodynamic effect before the first injection (whichever is longer), as well as the anticipated use of disallowed concomitant medication between the first injection and EoT/ET visit.
2. Previous use of any GM-CSF treatment and/or any treatment antagonising GM-CSF or its receptor at any time in the past.
3. The use of biological agents (as experimental therapy or not) within (whichever is longer):
- 10 times the respective half-life before the first injection of trial medication.

- the continuation of the pharmacodynamic effects of the respective agent before the first injection of trial medication.
- 3 months before the first injection of trial medication in case of TNF inhibitors.
- 12 months for any cell depleting therapies (after B-cell depleting therapy, B-cells must have returned to normal values before screening).
4. The use of the oral DMARD leflunomide within 12 weeks before the first injection of trial medication, or within 4 weeks before first injection of trial medication if supportive oral cholestyramine (>= 8 g/tid) or charcoal (>=50g/qds) washout treatment is/was given.
5. Chronic use of prophylactic or suppressive antibiotic, antifungal or antiviral agents.
6. The use of intra-muscular, intravenous or intra-articular corticosteroids within 4 weeks before the first injection of trial medication.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-08-2011
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MT203
Generic name:	N/A

Ethics review

Approved WMO Date:	29-10-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	04-02-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-03-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-01-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	09-02-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	17-07-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-12-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-12-2012

Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2010-018502-36-NL
CCMO	NL33507.058.10